DEPRESSION TREATMENT TODAY: CLINICAL FEATURES IN ANTIDEPRESSANTS' USE

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Antidepressant drugs were introduced into clinical practice in the mid-20th Century with TCA and MAO-I. The introduction of selective serotonin reuptake inhibitors (SSRIs) over twenty years ago had been the next major step in the evolution of antidepressants to develop drugs as effective as the TCAs but of higher safety and tolerability profile. During the past two decades SSRIs gained incredible popularity and have become the most widely prescribed medication in the psychiatric practice. The evolution of antidepressants continued resulting in introduction of selective and reversible monoamine oxidase inhibitors (eg. moclobemid), selective noradrenaline (eg. reboxetine), dual noradrenaline and serotonin reuptake inhibitors (milnacipram, venlafaxin, duloxetin) and drugs with distinct neurochemical profiles such as mirtazapine, nefazadone and tianeptine. While for the most part they have proven effective for the amelioration of depressive symptoms, they are associated with significant deficiencies. These well-recognized shortcomings have given impetus to the pursuit of new molecules that seek to improve on the efficacy, tolerability and safety of existing medications. Furthermore, approximately 30% of the population do not respond to current therapies and partial remission, residual symptoms and prevention of recurrence are hot issues. This has led to the development of new compounds with better efficacy, tolerability and safety.Agomelatine is a new antidepressant with an innovative pharmacological profile. It is a potent melatonergic agonist (MT(1) and MT(2)) and also has 5-HT(2c) antagonist properties. It improves depressive symptoms, sleep quality, anxiety. It has shown to have good profiles in tolerability and safety.The blockade of cortisol secretion continues to be a focus of attention for the development of new antidepressants. Thus, synthesis inhibitors, nonpeptide antagonists of corticotropin-releasing factor and glucocorticoid receptor antagonists show some promise in clinical and preclinical tests. Antagonists of the neuropeptide substance P, vasopressin and neuropeptide Y represent a departure of approach from traditional monoamine receptor-based mechanisms. While the clinical results with one substance P antagonist have led to the cessation of further trials, other molecules are in development. Approaches to treatment based on glutamatergic transmission, gabaergic transmission, intracellular messenger systems, transcription, neuroprotective and neurogenic factors, may provide an entirely new set of potential therapeutic targets, giving hope that further major advances might be anticipated in the treatment of depressive disorder soon.